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10/596,920	06/29/2006	Ties Van Bommel	DE040020	2337

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EXAMINER	
SCHLIENTZ, LEAH H	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,920	VAN BOMMEL ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/14/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 14 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e. results in a claim which is not a proper process under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. V. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. For example, there are no method steps recited in the "use of" claim.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of Application Serial No. 11/917,310. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to contrast agents comprising metal nanoparticles having acoustic impedance above 35.1^5 g/cm^{2}s and ultrasonic imaging methods therewith. The particles of the '310 Application are encapsulated in a non-proteinaceous biocompatible or biodegradable matrix particle and/or attached to a non-proteinaceous biocompatible or biodegradable matrix particle, the matrix of the matrix particles being selected from the group consisting of a

carbohydrate, a lipid, a synthetic polymer, an aqueous liquid, a surfactant and an organic liquid, or a mixture thereof. Claims 8 and 9 of the instant Application require a coating, which may be selected from natural or synthetic carbohydrates, synthetic polyaminoacids, or physiologically tolerable synthetic polymers or derivatives thereof. Accordingly, the claims are overlapping in scope and are obvious variants of one another.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Hainfeld *et al.* (US 6,818,199).

Hainfeld discloses metal nanoparticles that are useful for enhancing the contrast of x-rays or other radiation sources (abstract). In a preferred form is a medical imaging method and contrast agent which contrasts a targeted portion of a body of a living animal. The method includes intravenously administering a quantity of nanoparticles sufficient to contrast the targeted portion of the body under irradiation and irradiating

the targeted portion of the body with penetrating radiation. Each of the nanoparticles has a metallic core surrounded by a surface layer including a component having an affinity for the targeted portion of the body (column 4, lines 53+). The metal nanoparticles have a core composed of gold, platinum, palladium, thallium, bismuth, osmium, iridium, silver, tungsten, lead, tantalum, or uranium. The component of the material of the surface layer may be for example, an antibody, an antibody fragment, a peptide, a lipid, a carbohydrate, a nucleic acid, or a drug (column 5, lines 1-10). One such preferred gold compound synthesized and found to be useful is a gold nanoparticle with a gold core approximately 2 nm in diameter, which contains about 240 gold atoms. "Metal particle" or "metal nanoparticle" are defined to be all constructs having a metal core ranging from 0.5 to 500 nm in size. "Gold particle" or "gold nanoparticle" are defined to be all constructs having a gold core ranging from 0.5 to 500 nm in size. Larger or smaller gold compounds, clusters, particles and colloids may also be utilized, e.g. gold colloids that are typically characterized by their gold diameter (from 0.5 nm to 100 nm) (column 6, lines 8-20). The outer surface shell of material may include a directing moiety or more than one directing moiety for specific targeting, such as an antibody, antibody fragment, peptide, lipid, carbohydrate, nucleic acid, drug, or other molecule. In addition, it is possible to couple further components to the shell material. By such means, the directing moieties such as antibodies or peptides may be attached. They may be directly coupled to the core by attachment through a sulfur atom, for example; alternatively they may be covalently coupled to the organic shell; additionally, they may be adsorbed non-covalently to the particle or particle shell

(column 9, lines 50+). In addition to x-rays, other forms of electromagnetic probes may be employed to detect or image the agents. This includes, but is not limited to, the use of: static magnetic fields, visible light, lasers, ultrasound (column 19, lines 10-15).

It is noted that the limitation of the instant claims wherein the particle has "an acoustic impedance above 35.1^5 g/cm^{2}s" is not given patentable weight to distinguish over Hainfeld. "Products of identical chemical composition cannot have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or composition as that which is claimed, the properties applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The "discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." See *Atlas Power Co. v. Ireco Inc.*, 51 USPQ 2d 1943, 1947 (Fed. Cir. 1999). Therefore, merely claiming a new use, new function, or new property, which is inherently present in the prior art does not make the claim patentable. See *In re Best,* 195 USPQ 430, 433 (CCPA 1977), and MPEP § 2112. In the instant case, since Hainfeld teaches materials which have the same structural features as those claims, it is interpreted absent evidence to the contrary, that they would also have the claimed functional properties of acoustic impedance. This interpretation is supported by Applicant's specification, which teaches that acoustic impedance (Z) is defined as the product of density (p) and speed of sound (c) in a medium (paragraph 0028), and that examples of metals with an acoustical impedance

which is appropriate in the context of the present invention are gold, silver, platinum, palladium, tungsten or tantalum, rhenium, or a mixture thereof (paragraph 0029).

Claims 1-16 are rejected under 35 U.S.C. 102(e) as being anticipated by Oraevsky *et al.* (US 7,500,953).

Oraevsky discloses a method of enhancing detection for a specific object in a body. A nanoparticulate is administered to the body for location in an area to be explored for detection of the object, if present. The nanoparticulate is at least partially metallic, has a formed non-spherical shape having a minimal characteristic dimension in the range from about 1 to about 3000 nanometers, and has a formed composition capable of producing thermal pressure either in the nanoparticulate or in the object greater than the object could produce in the absence of the nanoparticulate. Electromagnetic radiation is directed into the body. The electromagnetic radiation has a specific wavelength or spectrum of wavelengths in the range from 300 nm to 300 mm selected so that the wavelength or wavelength spectrum is longer by a factor of at least 3 than the minimum characteristic dimension of the nanoparticulate. The nanoparticulate absorbs the electromagnetic radiation more than would one or more non-aggregated spherically shaped particles of the same total volume with a composition identical to the nanoparticulate. The nanoparticulate produces an enhanced optoacoustic signal resulting from the absorption that is received and converted into an electronic signal and presented for assessment of the at least one parameter by a human or a machine (abstract). Optoacoustic methods of imaging rely

not on detection of visible or infrared light irradiated onto a body, but on the sensitive detection of ultrasonic waves induced inside the body by optical radiation. Optoacoustic imaging fundamentally is based on the optical properties of the tissue it detects, but it relies on the sensitive detection of induced ultrasonic waves rather than light itself for image generation (column 1, lines 30-40). Gold nanoparticles are disclosed (column 7, lines 45+); including coated particles, e.g. PEG (column 8, lines 19+). Targeting vectors such as antibody may be attached. Therapeutic moieties such as drugs can be included (column 10). The body in which a specific object is detected in accordance with the detection method of this invention may be animate or inanimate and the specific object may be animate or inanimate. Thus, without limitation, in terms of medical significance, for example, the body may be an in vivo or in vitro specimen, and the object may be a molecule or a virus or bacterium. The body animate may be an animate human or non-human, and the object may be biological and comprise a specific tissue, cell, microorganism or molecule. For example, the object detected may be a tumor in an animate human or a physiologically operative molecule such as glucose, an enzyme, a protein receptor or a nucleic acid (column 11, lines 40+).

It is noted that the limitation of the instant claims wherein the particle has "an acoustic impedance above 35.1^5 g/cm^2s" is not given patentable weight to distinguish over Oraevsky. "Products of identical chemical composition cannot have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or composition as that which is claimed, the properties applicant discloses and/or claims are necessarily

present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The "discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." See *Atlas Power Co. v. Ireco Inc.*, 51 USPQ 2d 1943, 1947 (Fed. Cir. 1999). Therefore, merely claiming a new use, new function, or new property, which is inherently present in the prior art does not make the claim patentable. See *In re Best,* 195 USPQ 430, 433 (CCPA 1977), and MPEP § 2112. In the instant case, since Oraevsky teaches materials which have the same structural features as those claims, it is interpreted absent evidence to the contrary, that they would also have the claimed functional properties of acoustic impedance. This interpretation is supported by Applicant's specification, which teaches that acoustic impedance (Z) is defined as the product of density (p) and speed of sound (c) in a medium (paragraph 0028), and that examples of metals with an acoustical impedance which is appropriate in the context of the present invention are gold, silver, platinum, palladium, tungsten or tantalum, rhenium, or a mixture thereof (paragraph 0029).

Claims 1-7 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Bekeredjian *et al.* (*Ultrasond in Med. and Biol.*, 2002, 28(5), p. 691-695).

Bekeredjian discloses gold-bound microtubules as ultrasound contrast agent. Gold colloid was immobilized on protein microtubule walls. Gold-bound microtubules provide a persistent contrast effect, suggesting their use as an ultrasonic contrast agent

with the feasibility of antibody conjugation (abstract). Gold particles were 10 nm (page 692).

It is noted that the limitation of the instant claims wherein the particle has "an acoustic impedance above 35.1^5 g/cm^{2}s" is not given patentable weight to distinguish over Bekeredjian. "Products of identical chemical composition cannot have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure or composition as that which is claimed, the properties applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). The "discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." See *Atlas Power Co. v. Ireco Inc.*, 51 USPQ 2d 1943, 1947 (Fed. Cir. 1999). Therefore, merely claiming a new use, new function, or new property, which is inherently present in the prior art does not make the claim patentable. See *In re Best,* 195 USPQ 430, 433 (CCPA 1977), and MPEP § 2112. In the instant case, since Bekeredjian teaches materials which have the same structural features as those claims, it is interpreted absent evidence to the contrary, that they would also have the claimed functional properties of acoustic impedance. This interpretation is supported by Applicant's specification, which teaches that acoustic impedance (Z) is defined as the product of density (p) and speed of sound (c) in a medium (paragraph 0028), and that examples of metals with an acoustical impedance

which is appropriate in the context of the present invention are gold, silver, platinum, palladium, tungsten or tantalum, rhenium, or a mixture thereof (paragraph 0029).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hainfeld *et al.* (6,818,199), in view of .West *et al.* (US 2002/0103517).

Hainfeld discloses gold nanoparticles and methods of diagnostic imaging therewith including ultrasound, as set forth above.

Hainfeld does not specifically recite in vitro imaging. It is for this reason that West is joined.

West discloses localized delivery of heat and the localized imaging of biological materials. The delivery may be in vitro or in vivo and is useful for the localized

treatment of cancer, inflammation or other disorders involving overproliferation of tissue. The method is also useful for diagnostic imaging (abstract). Nanoparticles include gold-containing nanoparticles (see claim 5). Methods of diagnostic imaging of cell or tissue comprising the steps of delivering nanoparticles to the cell or tissue and exposing said nanoparticles to radiation selected from the group consisting of ultrasound, magnetic fields, and electric fields are disclosed (see claim 33).

It would have been obvious to one of ordinary skill in the art at the time of the invention to employ the particles of Hainfeld for methods of in vivo or in vitro imaging when the teaching of Hailfeld is taken in view of West. Both Hainfeld and West are directed to gold-containing nanoparticles and methods of imaging/therapy, including ultrasound. West teaches that structurally similar particles are useful for in vivo and in vitro imaging, and one would have been motivated to use the particles of Hainfeld for in vitro imaging of cells and tissues in order to expand the applications for which the particles are useful.

Claims 1-7 and 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bekeredjian *et al.* (*Ultrasond in Med. and Biol.*, 2002, 28(5), p. 691-695).

Bekeredjian discloses gold-bound microtubules as ultrasound contrast agent. Gold colloid was immobilized on protein microtubule walls. Gold-bound microtubules provide a persistent contrast effect, suggesting their use as an ultrasonic contrast agent with the feasibility of antibody conjugation (abstract). Gold particles were 10 nm (page 692).

It would have been obvious to one of ordinary skill in the art at the time of the invention to extend the teachings of Bekeredjian to in vivo/in vitro ultrasonic imaging, since Bekeredjian specifically teaches that his compositions are intended for use as ultrasound contrast agents, and one would have had a reasonable expectation of success in doing so since Bekeredjian teaches that his compositions provide advantages such as a persistent contrast effect.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS